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Original Article

RETINAL NERVE FIBER LAYER THICKNESS IN DIABETIC PATIENTS WITH AND WITHOUT DIABETIC RETINOPATHY

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ABSTRACT

Study aims to evaluate the retinal nerve fiber layer thickness in diabetic patients with and without retinopathy and to assess the correlation of retinal nerve fiber layer thickness among the cases diabetic retinopathy. A cross-sectional observational study was conducted at Department of Ophthalmology, PESIMSR, Kuppam during 2016–2019. Total 200 consecutive cataract known patients were selected based on SOP. Inclusion and exclusion criteria were employed to conduct the research work inclusion; all the patients with diabetes mellitus willing to give consent to clinical examination and evaluation. Exclusion; secondary glaucoma, patients who are mentally challenged, corneal and lenticular opacity, diabetic retinopathy with vitreous haemorrhage or retinal detachment and post retinal surgery. A total of 200 (400 eyes) cases were considered for the study group (G1:G2 = 100). Of which male comprises (61%) and females (39.0%), sex ratio 2:1. Diabetic status was recorded and it revealed that a total of 150 (75%) cases were subjected to diabetes and 50(25%) cases were subjected to non diabetes and it was found that the DM status is found to be statistically significant ($p < 0.01$). As per the findings, the average RNFL in the case of RE was 95.58 ± 6.96 in DM with DR and 98.08 ± 1.44 in DM without DR. It was found to be statistically significant ($p < 0.01$). In case of RNFL of LE was 95.80 ± 6.93 in DM with DR and 98.18 ± 1.48 in DM without DR, it was also found that there is a statistically significant ($p < 0.001$) with and without DR. The superior retinal nerve fibre layer thickness ($p < 0.001$), nasal retinal fiber layer thickness ($p < 0.001$), inferior retinal nerve layer thickness ($p < 0.001$), temporal nerve fibre layer thickness, macular thickness ($p < 0.001$), HBa1C ($p < 0.001$), serum creatine and serum cholestrol ($p < 0.001$) were found to be statistically significant. The present study concludes that the optical coherence tomography is an important non invasive tool for the assessment and quantification of the RNFL thickness in diabetes patients, while on evaluating for DR.

KEYWORDS: RNFL Thickness, Diabetic Retinopathy, DM & Fibre Thickness

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INTRODUCTION

Diabetes mellitus is one of the largest global health emergencies of the 21st century with more than 80% of cases being in the mid and low income group counties. Currently, number of cases worldwide is 415 millions and expected to become 640 million by 2040. The prevalence of diabetic between age 20 and 79 years is 6.2–7.40%. Diabetic retinopathy is one of the leading causes of visual loss and 5% of diabetic patients' progress to severe visual loss of 5/200 or less. Diabetic retinopathy is micoangiopathy resulting from chronic effects of the disease; the metabolic derangements have direct effect on neurons and support cells of the retina. Early neuronal damage particularly seen on spectral domain optical coherence tomography before the clinical evidence of diabetic retinopathy, in subjects with type 2 diabetes mellitus is said to be present. Thinning of retinal nerve fiber layer and ganglion cell layer in children with type 1 diabetes mellitus suggests that neurodegenerative changes occur in

presence of vascular changes. The evolution of newer technologies like the Heidelberg retina tomograph (HRT III) and OCT has made evaluation of the optic nerve head, the peripapillary area, the macular thickness and the RNFL thickness revolutionary. The resolution and reproducibilty of these technologies almost give us a near histopathological evaluation of the tissue or area we study in the retina. The newer findings in evaluating the potic nerve head (ONH) and retina include ONH and rim parameters, RNFL thickness along 3.2–3.4 mm diameter circle around the ONH and macular thickness. Recent studies with Heidelberg retina tomograph (HRT III) and optical coherence tomography demonstrated the thinning of retinal nerve fiber layer in patients with diabetic retinopathy. This study intended to highlight the OCT characteristics of the retinal nerve fiber layer in patients with diabetic retinopathy and to evaluate the association if any of, retinal nerve layer thickness with diabetic retinopathy. Early detection of retinal nerve fiber layer thinning is an useful tool in understanding the progression of diabetic retinopathy. The present study aims to evaluate the retinal nerve fiber layer thickness in diabetic patients with and without retinopathy to assess the relation of retinal nerve fiber layer thickness in diabetic retinopathy.

METHODS

A cross section observational study was conducted at Department of Ophthalmology, PESIMSR, Kuppam during 2016–2019. A total of 200 consecutive cataract known patients were selected based on SOP. Inclusion and exclusion criteria were employed to conduct the research work. Inclusion; all the patients with diabetes mellitus are willing to give consent to clinical examination and evaluation. Exclusion; secondary glaucoma, patients who are mentally challenged, corneal and lenticular opacity, diabetic retinopathy with vitreous haemorrhage or retinal detachment and post retinal surgery. The following procedure adopted for data collection patients with diabetes mellitus presenting with retinopathy was considered for the study. A detailed history which included demographic profile, information on past medical illness and drug intake for DM was extracted from the patients. The duration of diabetes was also recorded systematically. The Ocular diseases were recorded if any co morbidity was noticed by the patients, this data sets were collected in separate sheets. Ophthalmological examination was recorded in each eye individually which was included visual acuity and best corrected visual acuity, slit lamp examination, fundus examination, cup to disc ratio, applanation tonometry, visual field testing using Humhery field analyzer, retinal nerve fiber layer analysis was done for all the patients. HD OCT, blood sugar, HbA1C, serum cholestral and serum creatine were routinely done for all patients. The group of patients was categorized in the following ways viz. I^{st} group – Diabetic patients with retinopathy and 2^{nd} group was diabetes patients without retinopathy. Collected data were analyzed by using R software nominal scale. Multivariate analysis and logistic regression methods were employed to draw the significant inference.

RESULTS

Table 1: Age wise Distribution of Patients with Retinal nerve Fiber Layer Thickness in Diabetic Patients with and without Diabetic Retinopathy

Age Class	No	%	*P*-Value
40–45 years	38	19.01	≦0.0001
46–50 years	42	21.01	≦0.0001
51–55 years	35	17.51	≦0.0001
56–60 years	30	15.01	≦0.0001
61–65 years	22	11.01	≦0.0001
66–70 years	21	10.51	≦0.0001
>70 years	12	6.00	≦0.0001
Total	**200**	**100**	

Mean Age of the Patients was 54.73 ±7.48 Years

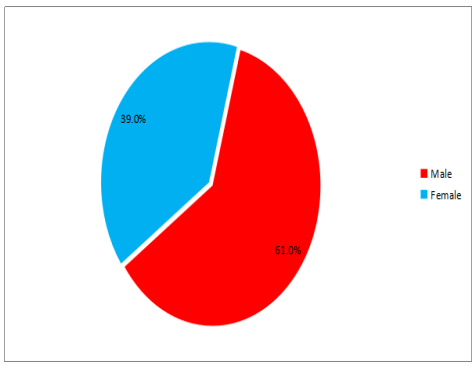

Figure 1.1: Gender Wise Distribution.

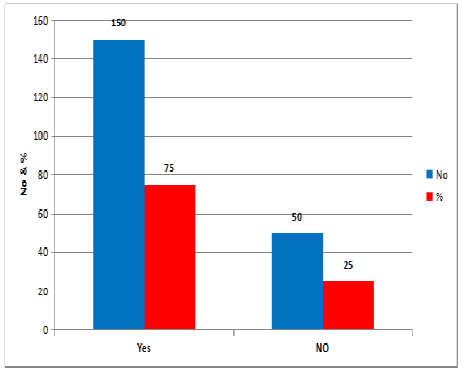

Figure 1.2: DM Status.

A total of 200(400 eyes) cases were considered for the study group (G1:G2=100). Of which male comprises 61.% and females 39.0%, sex ratio 2:1 (Figure 1.1). Diabetic status was recorded, it is revealed that a total of 150(75%) cases were subjected to diabetes and 50(25%) cases were subjected to non diabetes and it was found that the status was found to be statistically significant ($p < 0.01$). The age wise distribution was presented in table 1. It is depicted that, the mean age of the patients was 54.73 ± 7.48 years. Majority of the cases were found between the age group 46 and 50 years (21.01%) and less was found in >70 years (12.0%). All age group is found to be significantly correlated with diabetic retinopathy incidence ($p < 0.001$).

Table 2: Distribution of Duration

Duration	No	%	*P*-value
5 years	101	50.50	≦0.0001
6–10 years	18	9.00	≦0.0001
11–15 years	30	15.00	≦0.0001
>15 years	51	25.50	≦0.0001
Total	**200**	**100**	

Table 2 showed the duration of diabetes as per the resulted findings, the duration was categorized based on the mean and SD of the data sets, the mean duration was 9.5 years with SD 3.11. Majority of the patients were distributed 5 years 101(5.50%), 6–10 years 18 (9.0%), 11–15 years 30(15.0%) and >15 years 51 (25.50%). It was found that the duration is statistically significantly different with respect to retinopathy with and without ($p < 0.01$).

Table 3: Med OHA Distribution

Duration	med: OHA		*P*-value
	No	%	
5 years	106	53	≦0.0001
6–10 years	21	10.5	≦0.0001
11–15 years	38	19	≦0.0001
>15 years	35	17.5	≦0.0001
Total	**200**	**100**	

Table 3 showed the Med OHA distribution as per the resulted findings, the Med OHA distribution was categorized based on the mean and SD of the data sets, the mean duration was 9.55 years with SD 2.89. Majority of the patients were distributed 5 years 106(53.0%), 6–10 years 21(10.50%), 11–15 years 38(19.0%) and >15 years 35 (17.50%). It was found that the duration is statistically significantly different with respect to retinopathy with and without ($p < 0.01$).

Table 4: med: Insulin

med: Insulin	No	%	*P*-value
1–2 years	13	6.50	≦0.0001
3–4 years	25	12.50	≦0.0001
5–6 years	13	6.50	≦0.0001
>6 years	7	3.50	≧0.001
Nil	142	71.00	≧0.001
	200	**100**	

Table 4 showed the Med insulin distribution as per the resulted findings, the Med insulin distribution was categorized based on the mean and SD of the data sets, the mean duration was 5.52 years with SD 1.33. Majority of the patients were distributed 3–4 years 25(13.30%), 1–2 years 13(6.50%), 5–6 years 13(6.50%) and nil 142 (71.10%). It was found that the duration is statistically significantly different with respect to retinopathy with and without ($p < 0.01$).

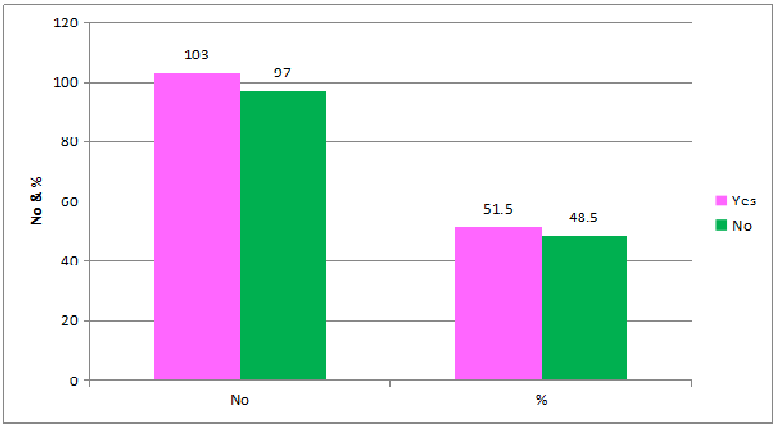

Figure 1.3: Family History.

Figure 1.3 depicted that the family history of the patients, 103(51.55%) showed family history of the diabetes, the correlation between family history and retinopathy was done by logistic regression, results was found to be statistically significant ($p < 0.01$).

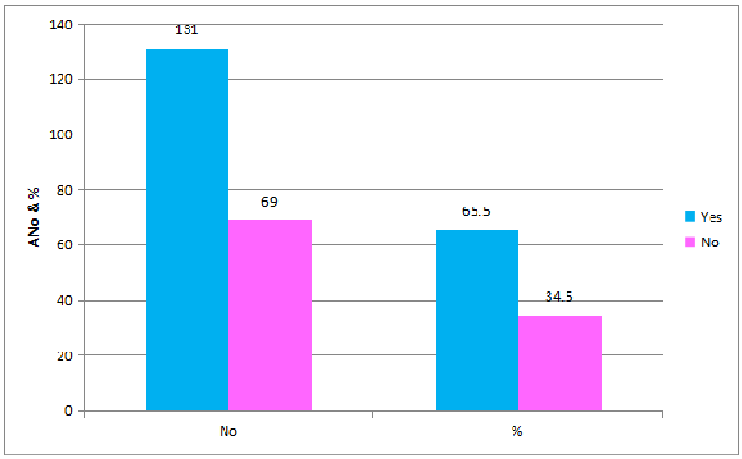

Figure 1.4: Hypertension Status.

Figure 1.4 depicted that the Hypertension status, 131 (65.50%) showed hypertensive history of the diabetes, the correlation between hypertensive and retinopathy was done by logistic regression, results was found to be statistically significant ($p < 0.01$).

Table 5: Correlation between Presence and absence of DM with Retinal Nerve Fiber layer Thickness in Diabetic Patients with and without Diabetic Retinopathy

Sl. No.	Parameters	DM-With (n = 151)	DM-Without (n = 49)	*P*-value
1	Age	56.72±9.99	48.57±5.42	0.000
2	Gender Male Female	87 64	35 14	0.012 0.036
3	Duration	11.15±8.10	-	0.082
4	Med OHA	10.38±7.37	-	0.011
5	med: Insulin	1.52±2.24	-	0.036
6	Family History	97	-	
7	Hyp	99	-	
8	Dialysis	33	-	

Table 5 defined the correlation between presence and absence of DM with retinal nerve fiber layer thickness in association DM with and without diabetic retinopathy, the correlation was done by multiple logistic regression, results revealed that the mean age of the with and without DM was 56.72 ± 9.99 years and 48.57 ± 5.42 years respectively, age was found to be statistically significant ($p < 0.01$). The parameters was correlated duration (11.15 ± 8.10 years) $p < 0.01$, Med OHA (10.38 ± 7.37) $p < 0.01$ med Insulin (1.52 ± 2.24) $p < 0.01$, family history, hypertension and dialysis when compared to with and without DM.

Table 6: Correlation between presence and absence of DM with Retinal Nerve Fiber Layer Thickness in Diabetic Patients with and without Diabetic Retinopathy

Sl	Parameters	DM-With (n = 150) **Mean** ± SD	DM-Without (n = 50) **Mean** ± SD	*P*-value
1	**BCVA RE**	0.45±0.22	1.00	0.008
2	**BCVA LE**	0.48±0.36	1.00	0.021
3	14.69±1.39	14.16±1.72	0.003	0.000
4	15.17±2.01	14.61±1.88	0.0122	0.000

There was a significant statistical difference among the group, the visual acuity was worsen in diabetic patients in association with retinopathy. The mean BCVA of RE of DM with DR was (0.45±0.22) and DM without DR was (1.00). Similar findings were noticed with the BCVA in the LE of DM with DR was (0.48 ± 0.36) and found to be statistically significant ($p < 0.01$). IOP is found to be statistically significant when compared to with and without DR ($p < 0.01$).

Table 7: Associated Parameters of Retinal Nerve Fiber Layer Thickness in Diabetic Patients with and without Diabetic Retinopathy

Parameters	With DM **Mean** ±SD	Without DM **Mean** ±SD	*P*-Value	Significant Level
CDR RE	0.49±0.07	0.48±0.08	0.1221	In significant
CDR LE	0.49±0.07	0.48±0.08	0.2236	Insignificant
RNFL RE(micrometers)	95.58±6.96	98.08±1.44	0.0361	Significant
RNFL LE(micrometers)	95.80±6.93	98.18±1.48	0.0112	Significant
S. RNFL RE(micrometers)	121.95±12.49	132.33±3.18	0.000	Significant
S. RNFL LE(micrometers)	122.93±11.74	132.16±3.13	0.000	Significant
T. RNFL RE(micrometers)	69.32±13.31	55.90±3.92	0.000	Significant
T. RNFL LE(micrometer)	69.87±13.28	55.47±3.87	0.000	Significant
N. RNFL RE(micrometers)	64.07±10.53	75.08±3.70	0.000	Significant
N. RNFL LE(micrometers)	62.76±8.53	73.98±3.53	0.000	Significant
I. RNFL RE(micrometers)	126.78±7.73	129.59±3.64	0.089	In significant
I. RNFL LE(micrometer)	127.73±8.06	130.69±4.01	0.098	In significant

MT RE(micrometer)	274.36±38.47	235.00±8.24	0.006	Significant
MT LE(micrometer)	273.52±35.81	235.67±4.89	0.001	Significant
FBS	104.48±20.58	73.37±5.33	0.008	Significant
PPBS	208.91±87.38	121.29±9.38	0.002	Significant
HBA1c	6.92±1.75	5.00±0.38	0.001	Significant
Sr cholestrol	160.81±17.02	143.80±10.76	0.001	Significant
Sr creatine	1.11±0.63	0.73±0.07	0.000	Significant

Table 7 summarizes the findings of associated parameters of DM with and without DR, the results revealed that CDR of the RE was 0.49 ± 0.07 in DM with DR and 0.48 ± 0.08 in DM without DR, it was found that statistically insignificant. The grading of diabetic retinopathy in DM with DR group (n = 150). The grading was done at ETDR classification. Moderate NPDR expressed was 48.0%, severe NPDR 19.0% and mild NPDR was 28% and PDR was 5% respectively. The average retinal nerve fibre layer among the groups was presented in table 7. As per the findings the average RNFL in the case of RE was 95.58 ± 6.96 in DM with DR and 98.08 ± 1.44 in DM without DR. It was found to be statistically significant ($p < 0.01$). In case of RNFL of LE was 95.80 ± 6.93 in DM with DR and 98.18±1.48 in DM without DR. It was also found to be statistically significant ($p < 0.001$) superior retinal nerve fibre layer thickness ($p < 0.001$) nasal retinal fiber layer thickness ($p < 0.001$), inferior retinal nerve layer thickness ($p < 0.001$), temporal nerve fibre layer thickness, macular thickness ($p < 0.001$), HBa1C ($p < 0.001$), serum creatine and serum cholestrol ($p < 0.001$) were found to be statistically significant.

DISCUSSIONS

The study highlights the probable chance on frequency of diabetic retinopathy in patients with diabetes mellitus and its correlation of duration of diabetes mellitus there found to increase the prevalence of DR in association with increased duration of DM similar results or findings done by Bansal et al. Duration of diabetics were more predisposed to develop the diabetic retinopathy changes and it was found to be statistically significant. The best corrected visual acuity (BCVA) of LE and RE among the groups highly significant difference was found in correlation with fiber thickness similar study reported by Hortensia S T et al. Concludes that the retinal thickness at the foveal centre correlated with best corrected visual acuity in normal and diabetic eyes and it was positively correlated. The measurement of macular thickness averages over eyes with the same visual acuity in patients with diabetes, both with and without evidence retinopathy and summarizes that visual acuity was significantly decreased in diabetic patients with retinopathy. Winfried et al. evaluated and quantify the macular and retinal thickness in diabetic retinopathy using optical coherence tomography as an objective and non invasive tool. Their observations was confirmed that the visual acuity in diabetic patients not only depends on edema formation at the foveal avascular zone but also on capillary destruction in the macula. They have summarily opined that the visual acuity is not a good predictor of retinal thickening and hence, the presence of macular edema suggests advanced stages of diabetic maculopathy. In our study, IOP was strongly associated with DR with nerve fiber thickness. Dielemans et al argued that IOP, high level of blood sugar are associated with elevated serum level and IOP. Mitchell P et al. studied that there is a significant and consistent association between diabetes and increased level of IOP, suggests that there is a real association between these two parameters. Pai-huei peng et al. did a study on nerve fiber thinning in patients with preclinical retinopathy and concluded that peripapillary retinal nerve fiber layer thickness was less in diabetic patients without vascular manifestations than healthy individuals. Farideh sharifipur et al. did a study on diural variations in intraocular pressure, central cornea thickness and macula and retinal nerve fiber layer thickness in diabetic patients and normal individuals the retinal nerve fiber thickness layer was significantly lower than the control group at all time points

[all *p*-values<0.05] as compared to the other parameters. Jay chhablani et al. did retrospective analysis of neurodegeneration in type 2 diabetes mellitus using spectral domain optical coherence tomography in age matched individuals. Diabetic patients were divided into three groups, 1st group no diabetic retinopathy, 2nd nonprolferative diabetic retinopathy and 3rd proliferative diabetic retinopathy. Average minimum and sectoral thickness ganglion cell inner plexiform layer and retinal nerve fiber layer were collected and the average and minimum ganglion cell inner plexiform layer showed significant thinning in diabetic subjects compared with controls in all stages of diabetic retinopathy [$p < 0.05$]. Early thinning on the inner retina happens in type 2 diabetics, even before visible vascular signs of diabetic retinopathy. This supports neurodegenerative process in eyes of diabetic patients. Stela Vujosevic et al. did a study on retinal layer changes in human preclinical and early clinical diabetic retinopathy support early retinal neural and muller cell alterations which showed decreased retinal nerve fiber layer thickness in diabetics without diabetic retinopathy or in initial diabetic retinopathy suggests an alteration in inner retina. Verma A et al did a study on neuronal damage precede vascular damage in subjects with type 2 diabetes mellitus and having no clinical diabetic retinopathy concluded that there was evidence of neural damage particularly on spectral domain optical coherence tomography before clinical evidence of diabetic retinopathy in subjects with type 2 diabetes mellitus. Chihara et al. photographed the retinal nerve fibre layer of the right eye of 137 patients with diabetes and 144 healthy control subjects. The findings suggest that the retinal nerve fibre layer abnormalities are common in patients with early diabetic retinopathy. Lopes de Faria and co-workers used the GDx nerve fiber analyzer to provide the first quantitative assessment of nerve fibre layer thickness in diabetics[12]. They demonstrated that the diabetic group has statistically significant thinning of the nerve fibre layer in the quadrant superior to the optic disc. Skarf B et al. points at the possibility of Retinal nerve fiber layer thickness measurement being helpful to detect early changes in diabetics.

CONCLUSIONS

The present study concludes that, the optical coherence tomography is an important non invasive tool for the assessment and quantification of the RNFL thickness in diabetes patients, while on evaluating for DR. The diabetes retinopathy (DR) is strongly associated with decreased level of retinal nerve fibre layer thickness. An Optical coherence tomography has considered in the merit of RNFL thickness at 3.4 mm from the disc margin, RNFL loss is one of the structural and functional changes of the retina, which is need to be addressed properly at right time.

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